

WHAT IS CLAIMED IS:

1. A method for production of a human proteinaceous therapeutic molecule:

(a) identify a mammalian cell line derived from a tissue that produces the proteinaceous therapeutic molecule in nature;

5 (b) transfecting a plurality of cells from the mammalian cell line with a gene coding for the human proteinaceous therapeutic molecule;

(c) cloning the transfected cells expressing the human proteinaceous therapeutic molecule;

10 (d) expanding the cloned cells in a rotating cell culture system filled with a culture media, wherein the rotating cell culture system provides a simulated micro-gravity environment for the expanding cloned cells;

(e) separating a volume of culture media from the expanded cloned cells; and

(f) isolating a protein fraction from the volume of culture media, wherein the protein fraction is rich in the proteinaceous therapeutic molecule.

15 2. The method of claim 1, wherein the human proteinaceous therapeutic molecule is post-translationally modified.

3. The method of claim 1, wherein the human proteinaceous therapeutic molecule is PP14.

20 4. The method of claim 1, wherein the mammalian cell line is a human derived cell line.

5. The method of claim 3, wherein the mammalian cell line is a human myelomous leukemia cell line.

6. The method of claim 1, wherein the gene coding for the human proteinaceous therapeutic molecule includes a bioselection mechanism.

5 7. The method of claim 5, wherein the bioselection mechanism is an antibiotic resistance.

8. The method of claim 1, wherein the gene coding for the human proteinaceous therapeutic molecule includes a polyhistidine fusion tag.

10 9. The method of claim 1, wherein the rotating cell culture system provides a low-shear environment equal to 2 dynes/cm² or less.

10. The method of claim 1, wherein the rotating cell culture system rotates from about 10 rpm to about 20 rpm.

11. The method of claim 1, wherein the rotating cell culture system is transversed by a membrane carrier having a molecular weight cut-off membrane mounted thereon.

15 12. The method of claim 11, wherein the molecular weight cut-off membrane has a molecular weight cut-off value that is greater than the molecular weight of the human proteinaceous therapeutic molecule.

20 13. The method of claim 11, wherein the molecular weight cut-off membrane has a molecular weight cut-off value that is less than the molecular weight of the human proteinaceous therapeutic molecule.

14. The method of claim 1, further comprising the step of providing a continuous flow of the culture media to the cloned cells in the rotating cell culture system.

15. The method of claim 14, wherein the continuous flow of culture media is oxygenated through an external gas exchange membrane.

16. The method of claim 1, wherein the protein fraction is isolated using a column material designed to remove serum albumin from the culture media.

5 17. The method of claim 8, wherein the protein fraction is isolated using a metal chelate column.

18. A method for the production of recombinant human proteins comprising:

(a) selecting a post-translationally modified human protein;

10 (b) identifying a human cell line derived from a tissue that produces the human protein;

(c) transfecting a plurality of cells from the human cell line with a gene coding for the human protein and a gene coding for a bioselection mechanism;

(d) cloning the transfected cells expressing the human protein and the bioselection mechanism;

15 (e) introducing the cloned transfected cells into a rotating cell culture system filled with a culture media; and

(f) growing the cloned transfected cells in the rotating cell culture system, wherein the cloned cells synthesize the human protein and excrete the human protein into the culture media in the rotating cell culture system.

20 19. The method of claim 18, wherein the human protein is PP14.

20. The method of claim 18, wherein the human cell line is human myelomous leukemia cell line.

21. The method of claim 18, wherein the bioselection mechanism is an antibiotic resistance.

5 22. The method of claim 18, wherein the rotating cell culture system is transversed by a membrane carrier having a molecular weight cut-off membrane mounted on the membrane carrier.

23. A method for the production of recombinant human proteins comprising:

(a) selecting a post-translationally modified human protein;

10 (b) identifying a human cell line derived from a tissue that produces the human protein;

(c) transfecting a plurality of cells from the human cell line with a gene coding for the human protein and a bioselection mechanism;

15 (d) cloning the transfected cells expressing the human protein and the bioselection mechanism;

(e) providing a horizontally rotating cell culture system having a molecular weight cut-off membrane transversing a growth chamber of the cell culture system, wherein the rotating cell culture system provides a low shear environment less than or equal to 2 dynes/cm²;

20 (f) introducing the cloned transfected cells into the growth chamber of the rotating cell culture system filled with a culture media;

(g) maintaining a flow of the culture media through the growth chamber of the rotating cell culture system;

(h) expanding the cloned transfected cells in the rotating cell culture system, wherein the cloned cells synthesize the human protein and excrete the human protein into the culture media in the rotating cell culture system;

(i) separating the cloned transfected cells from a volume of the culture media containing the excreted human protein; and

(j) isolating a protein fraction from the volume of the culture media, wherein the protein fraction is rich in the human protein.

10 24. The method of claim 23, wherein the molecular weight cut-off membrane has a molecular weight cut-off value that is less than a molecular weight of the human protein.

25. The method of claim 24, wherein the human protein accumulates in the growth chamber of the rotating cell culture system.

15 26. The method of claim 23, wherein the protein fraction is isolated using a column material designed to bind and remove albumin from the volume of culture media without binding and removing the human protein from the volume of culture media.